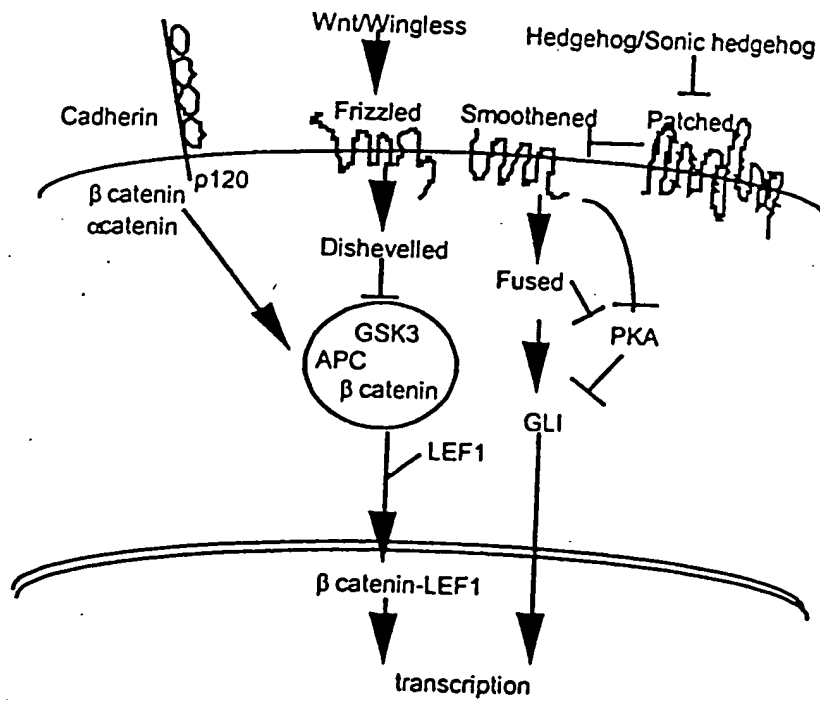


Figure 1



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Figure 2a

Alignment of several frizzled family members

	→	amino terminal domain
fz3/mouse	-----	MAVSWIVFDLWLLTVFLG---QIGGHS-----LFSCE
fz4/mouse	-----	MAWPGTGPS---SRGAPGGVGLRLGLLLQFLLLRPTLGFGLD---EEERRCD
fz8/mouse	-----	MEWGYL-----LEVTSLLAALAVLQRSSG-AAAASAK-----ELACQ
fz5/human	-----	MARPDP-----SAPPSLL--LLLLAQLVG-RAAAASK-----APVCQ
fzd9/human	-----	MAVAPLRGALLLWQLLAAGGALEIGRFD-----PERGRG-----AAPCQ
fz1/rat	LEAPLLLG	VRAQPAG---QVSG-PGQQRPPPPQPQGG--QQYNGERG--ISIPDHGYCQ
fz2/rat	-----	MRARSAL---PRSALPRLLPLLLLPAAGP--AQFHGEKG--ISIPDHGFQ
fz/Dros	ILPTLIQGV	QRYDQS---PLDASPYRSGGGLMASSG---TELDG-----LPHHNRCE
fz2/Dros/	GLVLLLT	SCRADGPL-----HSADHGMGGMGMGGHGLD-ASPAPGYGVPAIPKDPNLRCE
		* :
		CRD
fz3/mouse	PITLRMCQDL	PYNTTFMPNLLNHYDQQTAAALAMEPFHPMVNLDCSRDFRPFILCALYAPIC
fz4/mouse	PIRIAMCQNL	GYNVTKMPNLVGHLELQTDALQLTFTPLIQYGCSSQLQFFLCSSVYVPMC
fz8/mouse	EITVPLCKG	IGYNYTYMPNQFNHDTQDEAGLEVHQFWPLVEIQCSPLDKFFLCSMYTPIC
fz5/human	EITVPMCRG	IGYNLTHMPNQFNHDTQDEAGLEVHQFWPLVEIQCSPLDRFFLCMTYTPIC
fzd9/human	AVEIPMCRG	IGYNLTRMPNLLGHTSQGEAAAEAEFAPLVQYGCCHSLRFFLCSLYAPMC
fz1/rat	PISIPLC	TDIAYNQTIMPNLLGHTNQEDAGLEVHQFYPLVKVQCSAELKFFLCSMYAPVC
fz2/rat	PISIPLC	TDIAYNQTIMPNLLGHTNQEDAGLEVHQFYPLVKVQCSPELRFFLCSMYAPVC
fz/Dros	PITISICKN	IPYNMTIMPNLIGHTKQEEAGLEVHQFAPLVKIGCSDDLQLFLCSLYVPVC
fz2/Dros/	EITIPMCRG	IGYNMTSFPNEMNHETQDEAGLEVHQFWPLVEIKCSPDLKFFLCSMYTPIC
	:	: * : * : * : * : * : * : * : * : * : * : * : *
		CRD
fz3/mouse	M-EYGRVTL	PCRRLCQRAYSECSKLMEMFG-VPWPEDMECSRFPDCE-EPYPRLVDLN--
fz4/mouse	TEKINIP	IGPCGGMCLSVKRRCEPVLREFG-FAWPDTLNCSKFPPQN-DHNHMCMEGP--
fz8/mouse	LEDYKKPL	PPCRSVCERAKAGCAPLMRQYG-FAWPDRLMRCDRLPEQG-NPDTLCMDYN-R
fz5/human	LPDYHKPL	PPCRSVCERAKAGCSPLMRQYG-FAWPERMSCDRLPVLGRDAEVLCDYN-R
fzd9/human	TDQVSTP	IPACRPMCEQARLRCAIMEQFN-FGWPDSDLCARLPTRN-DPHALCMEAPEN
fz1/rat	T-VLEQAL	PPCRSLCERA-QGCEALMNKFG-FQWPDTLKCEKFPVHG--AGELCVGQNTS
fz2/rat	T-VLEQA	IPPCRSLCERARQGCEALMNKFG-FQWPERLRCEHFPVHG--AEQICVGNHS
fz/Dros	T-ILERP	IPPCRSLCESA-RVCEKLMKTYN-FNWPENLECSKFVHG--GEDLCVAENTT
fz2/Dros/	LEDYHKPL	PVCRSVCERARSGCAPIMQQYS-FEWPERMACEHLPLHG-DPDNLCMEQPSY
		* : * : * : * : * : *
		CRD
fz3/mouse	-----	LVGDPTDTE---
fz4/mouse	---GDEE-	-----VPLPHKTP-
fz8/mouse	TDLTAAAP	SPRRRLPPPPPPGEQPPSGSGHSRPPGARPPHRGGSSRGSGDAAAAPPSRGG
fz5/human	SEATTAP	PRP---FPAKP---TLP--G-----PP-----G-----APAS--GG
fzd9/human	ATAGPAE	PHK---GLGM---LP-----VAPRPAPPPG
fz1/rat	DKGTPT	PSL-----L-----PEFWTSNPQHG
fz2/rat	EDG--TP	AL-----L-----TTAPPSGLQPG
fz/Dros	SSA-----	STAATPTRSVA
fz2/Dros/	TEAGSGG	SSG---GSGG---SGSGSGSGGKRKQGGSGSGSGAGSSSGSTSTKPCR--GR

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Figure 2b

amino terminal domain continued

	← TM1 →
fz3/mouse	YSFLHVRDCSPPCPN-----MYFREELSFARYFIGLISIICLSATLFTFLTLIDVTR
fz4/mouse	--LNCVLKCGYDAG-----LYSRSAKEFTDIWMMAVWASLCFISTTFTVLTFLIDSSR
fz8/mouse	-KTGQIANCALPCHN-----PFFSQDERAFTVFWIGLWSVLCFVSTFATVSTFLIDMER
fz5/human	-RTGQVPNCAVPCYQ-----PSFSADERTFATFWIGLWSVLCFISTTTVATFLIDMDT
fzd9/human	--RSCAPRCGPGEV-----FWSRRDKDFALVWMAVWSALCFFSTAFTVLTFLLEPHR
fz1/rat	LGEK---DCGAPCEPTKVYGLMYFGPEELRFSRTWIGIWSVLCCASTLFTVLTLYLDMRR
fz2/rat	LGER---DCAAPCEPARPDGSMFFSHHTRFARLWILTWSVLCCASTFTTTSVLAMQR
fz/Dros	VGGKDLHDGAPCH-----AMFFPERERTVLRVWVGSAAVCVASCLFTVLTFLIDSSR
fz2/Dros/	QRIAGVPNCGIPCKG-----PFFSNDEKDFAGLWIALWSGLCF CSTLMTLTFTFIIDTER
	* : : * : *

	← TM2 →	extracellular domain loop 1
fz3/mouse	FRYPERPIIFYAVCYMMVSLIFFIGFLE-DRVACNASSP-----	
fz4/mouse	FSYPERPIIFLSMCYNIYSIAYIVRLTVGRERISCDF-----	
fz8/mouse	FKYPERPIIFLSACYLFSVSVGYLVRLVAGHEKVACSGGAPGAGGRGGAGGAAAAGAGAAG	
fz5/human	FRYPERPIIFLSACYLFSVSVGYLVRLVAGHASVACS-----	
fzd9/human	FQYPERPIIFLSMCYNVYSLAFLIRAVAGAQSVACD-----	
fz1/rat	FSYPERPIIFLSGCTAVAVAYIAGFLE-DRVVCNDKFAE-----	
fz2/rat	FRYPERPIIFLSGCTMVSVAYIAGFVLQ-ERVVCNERFSE-----	
fz/Dros	FRYPERAIVFLAVCYLVVGCAYVAGLGAG-DSVSCREPFPPPVK---LG-----	
fz2/Dros/	FKYPERPIVFLSACYFMVAVGYLSRNLQNEEIACDG-----	
	* **** : : * . * . . .	

	← TM3 →
fz3/mouse	-----AQYKASTVTQGSNK-ACTMLFMVLYFFTMAGSVWVILTITWFLA
fz4/mouse	-----EEAAEPVLIQEGLKNTGCAIIFLLMYFFGMASSIWWVILTITWFLA
fz8/mouse	RGASSPGARGEYEELGAVEQHVRVYETTGPACTVVFLLVYFFGMASSIWWVILSLTWFLA
fz5/human	R-----EHNHIHYETTGPACTIVFLLVYFFGMASSIWWVILSLTWFLA
fzd9/human	-----QEAGALYVIQEGLENTGCTLVFLLLYFFGMASSIWWVILTITWFLA
fz1/rat	-----DGARTVAQGTKKE-GCTILFMMLYFFSMASSIWWVILSLTWFLA
fz2/rat	-----DGYRTVGQGTKKE-GCTILFMMLYFFSMASSIWWVILSLTWFLA
fz/Dros	-----RLQMMSTITQHRQTTCTVLFMALYFCCMAAFWWSCLAFAWFLA
fz2/Dros/	-----LLLRESSTGPHSCTLVFLLTYFFGMASSIWWVILTITWFLA
	: * : : : * : : : *

	← TM4 →	extracellular domain loop 2←
fz3/mouse	AVPKWGSEAIEKKALLFHASAWGIPGTLTIILLAMNKIEGDNISGVCVGLYDVDAALRYF	
fz4/mouse	AGLKWGHEAIEMHSSYFHIAAWAIPAVKTIVILIMRLVDADELTLGCVGNQNLDAITGF	
fz8/mouse	AGMKWGNEAIAIGYSQYFHLAAWLVPVKSIAVLALSSVDGDPVAGICYVGNQSLDLNRGF	
fz5/human	AAMKWGNEAIAIGYQYFHLAAWLIPVKSITALALSSVDGDPVAGICYVGNQNLNLRGF	
fzd9/human	AGKKWGHEAIEAHGSYFHMAAWGLPALKTIVILTLRKVAGDELTLGCVVASTDAAALTGF	
fz1/rat	AGMKWGHEAIEANSQYFHLAAWAVPAIKTITILALGQVDGDLVSGVCFVGLNNDALRGF	
fz2/rat	AGMKWGHAAIEANSQYFHLAAWAVPAVKTITILAMGQIDGDLVSGVCFVGLNRLDPLRGF	
fz/Dros	AGLKWGHEAIEENKSHLFLVAVAVPALQTIISVLALAKVEGDILSGVCFVGLDTHSLGAF	
fz2/Dros/	AGLKWGNEAITKHSQYFHLAAWLIPVQSVAVLLLSAVDGDPIGICYVGNLNPDLKTF	
	: ** . * : . ** ** * . : * : : : * : : *	

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TM5

fz3/mouse	VLAPLCLYVVVGVSLLLAGIISLNRVRIEIPLEKE----	NQDKLVKFMIRIGVFSILYL
fz4/mouse	VVAPLFTYLVIIGTLFIAAGLVALFKIRSNLQK-DG----	TKTDKLERLMVKIGVFSVLYT
fz8/mouse	VLAPLVIYLFIGTMFLLAGFVSLFRIRSVIKQGGP----	TKTHKLEKLMIRLGLFTVLYT
fz5/human	VLGPLVLVLYLVGTFLFLLAGFVSLFRIRSVIKQ-GG----	TKTDKLEKLMIRIGIFTLLYT
fzd9/human	VLVPLSGYLVLGSSFLLTGFVALFHIRKIMKT-GG----	TNTEKLEKLMVKIGVFSILYT
fz1/rat	VLAPLFVYLFIGTSFLLAGFVSLFRIRTIMKH-DG----	TKTEKLEKLMVRIGVFSVLYT
fz2/rat	VLAPLFVYLFIGTSFLLAGFVSLFRIRTIMKH-DG----	TKTEPLERLMVRIGVFSVLYT
fz/Dros	LILPLCIYLSIGALFLLAGFISLFRIRTVMKT-DG----	KRTDKLERLMRIGFFSGLFI
fz2/Dros/	VLAPLFVYLVIGTTFLMAGFVSLFRIRSVIKQGGVGAGVKADKLEKLMIRIGIFSIVLYT	
	: * : * : * : * : * : * : *	
	TM6	extracellular domain loop 3
fz3/mouse	VPLLVVIGCYFYEQAYRGIWETTWIQERCREYHIPCYPQVTQMS-----	RPDLILFLM
fz4/mouse	VPATCVIACYFYEISNWALFRYSADDS-----	NMAVEML
fz8/mouse	VPAAVVACLFYEQHNRPRWEATHNCPCLRDLPDQARR-----	PDYAVFML
fz5/human	VPASIVVACLYEQHYRESWEAALTCACPGHDTGQPRAK-----	PEYVWLML
fzd9/human	VPATCVIVCYVYERLNMDFWRLRATEQPCAAAAGPGGRDCSLP----	GGSVPTVAVFML
fz1/rat	VPATIVIACYFYEQAFRDQWERSWVAQSKSYAIPCPHLQGGGGVPPHPMSPDFTVEMI	
fz2/rat	VPATIVIACYFYEQAFREHWERSWVSQHKSLAIPCPAHYT-----	PRTSPDFTVYMI
fz/Dros	LPAVGLLGCLFYEYYNFDEWMIQWHRDICKPFSIPCPAARAPGS----	PEARPIFQIFMV
fz2/Dros/	VPATIVIGCYLYEAAAYFEDWIKALACPCAQVK--GPGKK-----	PLYSVLML
	* : . . *	:
	TM7	
fz3/mouse	KYLMALIVGIPSIFVVGSKKTCFEWASFFHGRRKKEIVNESRQVLQEPDFAQSLLRDPNT	
fz4/mouse	KIFMSLLVGITSGMWIWSAKTLHTWQKCS-----	NRLVNSGKVK----REKRG
fz8/mouse	KYFMCLVVGITSGVWVWSGKTLESWRALC-----	TRCCWASKGAAGVAGAGGSG
fz5/human	KYFMCLVVGITSGVWVWSGKTLESWRRFT-----	SRCCCRPR-----RGHK-
fzd9/human	KIFMSLVVGITSGVWVWSKTFQTWQSLC-----	YRKIAAGRARA----KACRA
fz1/rat	KYLMTLIVGITSGFVIWSGKTLNSWRKFY-----	TRLTNSK-----QGETT
fz2/rat	KYLMTLIVGITSGFVIWSGKTLHSWRKFY-----	TRLTNSR-----HGETT
fz/Dros	KYLCMSLVGVTSSVWLYSSKTMVSWRNFF-----	ERLQGEKPT----RAQAY
fz2/Dros/	KYFMALAVGITSGVWVWSGKTLESWRRFW-----	RRLLGAPDRTGANQALIKQR
	: : * : * : *	

Figure 3

Sequence alignment of a portion of the aminoterminal extracellular region of human Frizzled receptors

HFZ1 VGQNTSDKGT---PSLLPEFWTSNPQHGGGGHGRG-----GFPGGAG----ASERGKFSCPR
 HFZ2 VGQNHSEDGA----PALLTTAPPPGLQPGAGGTPG-----GPGGGGAPPRYATLEHPFHC
 HFZ3 LVDLNLAG-----EPTEGAPV-----AVQRDYG-----FWC
 HFZ4 CMEGPGD-----EE-----VPLPHKTPI-----QP
 HFZ5 CMDYNRSEATTAPPRPFPKPTLPG-----PPGA-----PASGG-----ECPAGGPFV-----CKC
 HFZ6 TFDPHTEF-----LGPQKKTE-----QVQRDIG-----FWC
 HFZ7 VGQNTSDGSGGPGGGPTAYPTAPYLPDLPFTALPPG-----ASDGRGRPAF-----PFSC
 HFZ8 CMDYNRTDLTTAAPSPPRRLPPPPP-GEQPPSGSGHGRPPGARPPHRGGGRGGGGGDAAPPARGGGGGGKARPPGGGAAP---CEPGCQC
 HFZ9 CMEAPENA-TAGPAEPHKGLGMLPV-----APRPARPPG-----DLGP
 HFZ10 NYLCMEAPNN---GSDEPTRGSGLFPP-----LFRPQRPHSAQ----EHP

Figure 4

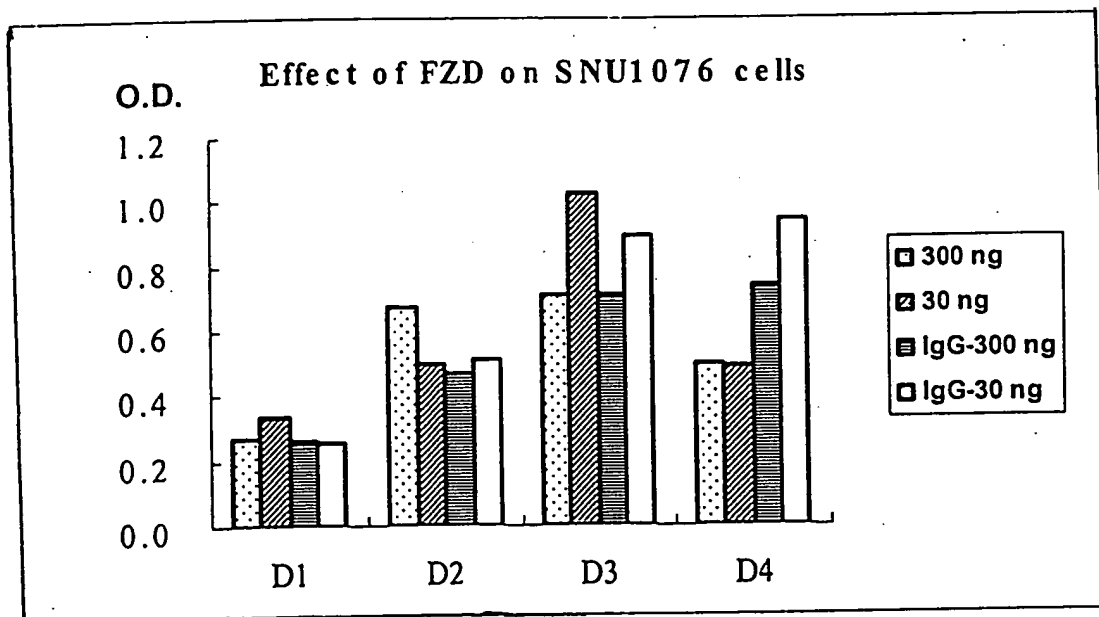
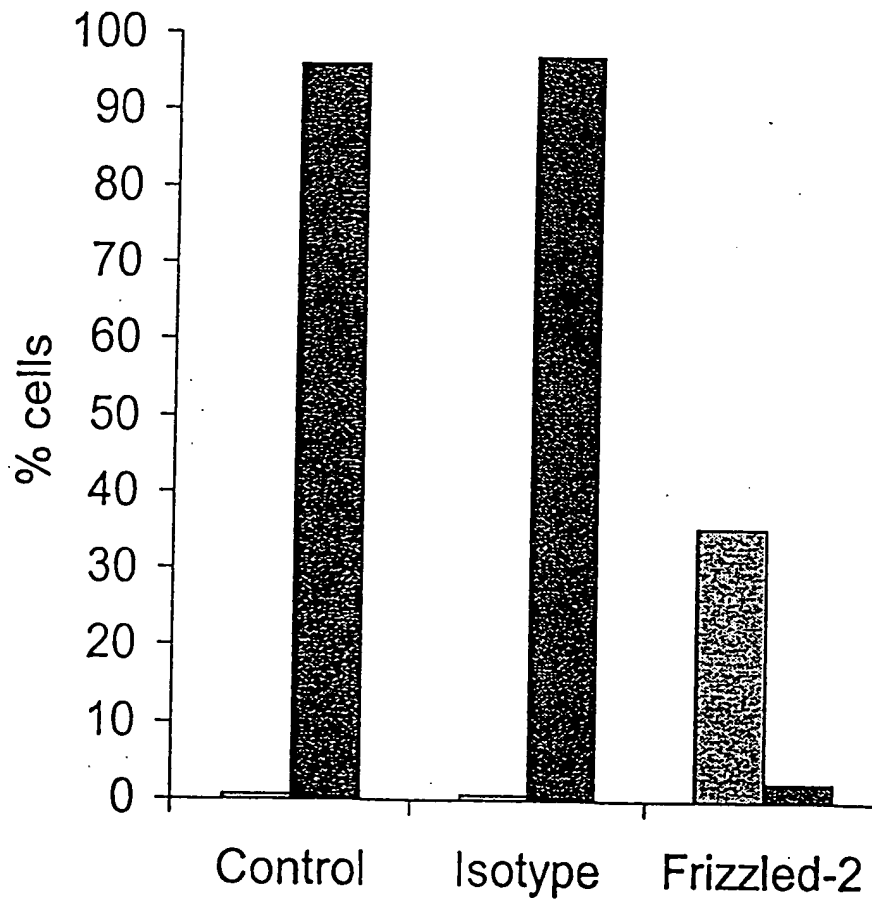


Figure 5

Effect of antibodies SNU 1076 Cells



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Figure 6

Effect of antibodies on SNU 1076 cells

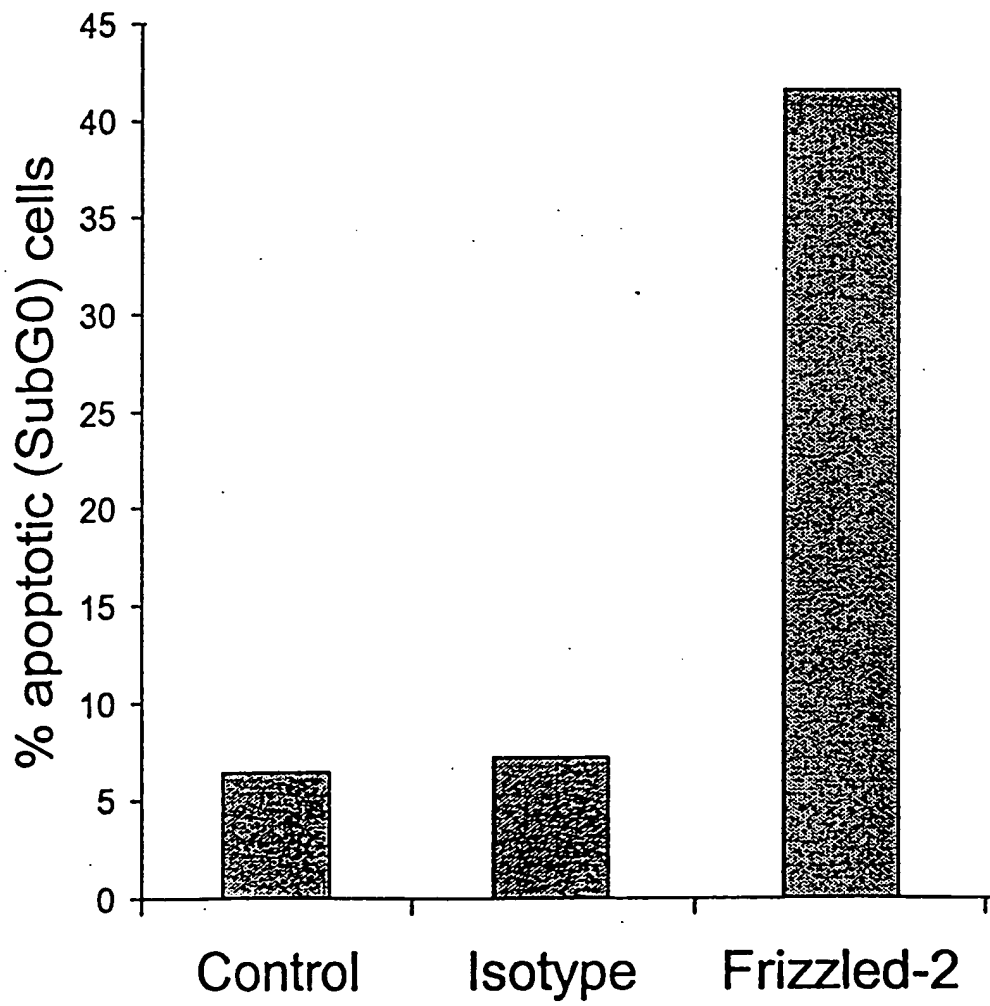


Figure 8a

→ amino terminal domain

HFZ1	MAEEEAPKKSRAAGGGASWELCAGALSARLAEEGSGDAGGRRRPPVDPRRLARQLLLLLLW
MFZ1	MAEEAAPSESRAAGR-LSLELCAEALPGRREEVGHEDTASHRRPRADPRRWASGLLLLLLW
HFZ2	-----MRPRSALPRLLLPLL
HFZ3	-----MAMTWIVFSLWPLTV
MFZ3	-----MAVSWIVFDLWLLTV
HFZ4	-----MAWRGAGPSVPGAPGGVGLSLGLLLO
MFZ4	-----MAWPGTGPSSRGAPGGVGLRLGLLLO
HFZ5	-----MARPDPSAPPSLL--LLL
HFZ6	-----MEMFTFLLTCI
MFZ6	-----MERSPFLLACI
HFZ7	-----MRDPGAAAPLSSSLGLCALVLA
MFZ7	-----MRGPGTAASHSPGLCALVLA
HFZ8	-----MEWGYLLEVTSLLAALAL
MFZ8	-----MEWGYLLEVTSLLAALAV
HFZ9	-----MAVAPL-RGALLLWQLLA
MFZ9	-----MAVPPLLRGALLLWQLLA
HFZ10	-----MQRPGPRLWLVLQ

HFZ1	LLEAPLLLGVRAQAAGQGPGPGGQPPPPPPQQQSGQQYNGERGISVPDHGYCQPIS
MFZ1	LLEAPLLLGVRAQAAGQVSG---PGQQAPPPPPQQQSGQQYNGERGISIPDHGYCQPIS
HFZ2	LLPA-----A-----GPAQFHGEKGISIPDHGFCQPIS
HFZ3	FMGHI-----GGHSLFS-----CEPIT
MFZ3	FLGQI-----GGHSLFS-----CEPIT
HFZ4	LLLLLG-----PARGFGDEEE-----RRCDFIR
MFZ4	FLLLLR-----PTLGFGEDEE-----RRCDFIR
HFZ5	LAQLVG-----RAAAASKAPV-----CQEIT
HFZ6	FLPLL-----RGHSLFT-----CEPIT
MFZ6	LLPLV-----RGHSLFT-----CEPIT
HFZ7	LLGAL-----SAGAGAQPYHGEKGISVPDHGFCQPIS
MFZ7	LLGAL-----PTDTRAQPYHGEKGISVPDHGFCQPIS
HFZ8	LQRSSG-----AAAASAKELA-----CQEIT
MFZ8	LQRSSG-----AAAASAKELA-----CQEIT
HFZ9	AGGAAL-----EIGRFDPERGR---GAAPCQAVE
MFZ9	TGGAAL-----EIGRFDPERGR---GPAPCQAME
HFZ10	VMGSCA-----AISSMDMERP---GDGKCQPIE

*: :

HFZ1	IPLCTDIAYNQTIMPNLLGHTNQEDAGLEVHQFYPLVKVQCSAELKFFLCSMYAPVCT-V
MFZ1	IPLCTDIAYNQTIMPNLLGHTNQEDAGLEVHQFYPLVKVQCSAELKFFLCSMYAPVCT-V
HFZ2	IPLCTDIAYNQTIMPNLLGHTNQEDAGLEVHQFYPLVKVQCSPELRFLLCSMYAPVCT-V
HFZ3	LRMCQDLPYNTTFMPNLLNHYDQQTAAALAMEPFHPMVNLDCSRDFRPFLLCALYAPICM-E
MFZ3	LRMCQDLPYNTTFMPNLLNHYDQQTAAALAMEPFHPMVNLDCSRDFRPFLLCALYAPICM-E
HFZ4	ISMCONLGYNVTKMPNVLGHQLQTDALQLTTFTPLIQYGCSSQLQFFLCVYVPMCTEK
MFZ4	IAMCONLGYNVTKMPNVLGHQLQTDALQLTTFTPLIQYGCSSQLQFFLCVYVPMCTEK
HFZ5	VPMCRGIGYNLTHMPNQFNHDTQDEAGLEVHQFWPLVEIQCSFDLRFLLCTMYTPICLPD
HFZ6	VPRCMKMYNMTFFPNLMGHYDQGSIAAVEMEHFLPLANLECSNIEFLCKAFVPTCI-E
MFZ6	VPRCMKMYNMTFFPNLMGHYDQGSIAAVEMGHFLHLANLECSNIEFLCKAFIPTCT-E
HFZ7	IPLCTDIAYNQTIMPNLLGHTNQEDAGLEVHQFYPLVKVQCSPELRFLLCSMYAPVCT-V
MFZ7	IPLCTDIAYNQTIMPNLLGHTNQEDAGLEVHQFYPLVKVQCSPELRFLLCSMYAPVCT-V
HFZ8	VPLCKGIGYNYTYPNQFNHDTQDEAGLEVHQFWPLVEIQCSFDLKFLLCSMYTPICLD
MFZ8	VPLCKGIGYNYTYPNQFNHDTQDEAGLEVHQFWPLVEIQCSFDLKFLLCSMYTPICLD

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Figure 8b

HFZ9 IPMCRGIGYNLTRMPNLLGHTSQGEAAAELAEFAPLVQYGCNLSHLRFFLCSLYAPMCTDQ
 MFZ9 IPMCRGIGYNLTRMPNLLGHTSQGEAAAQLAEFSPLVQYGCNLSHLRFFLCSLYAPMCTDQ
 HFZ10 IPMCKDIGYNMTRMPNLMGHENQREAAIQLHEFAPLVEYGCNLSHLRFFLCSLYAPMCTEQ
 : * : ** * : ** . * * * : : * : : * . . . *** : * *

HFZ1 LEQALPPCRSLCERARQGCEALMNKFGFQWPDTLKCEKFPVHG--AGELCVGQNTSDKGT
 MFZ1 LEQALPPCRSLCERARQGCEALMNKFGFQWPDTLKCEKFPVHG--AGELCVGQNTSDKGT
 HFZ2 LEQAIPPCRSICERARQGCEALMNKFGFQWPERLRCEHFPRHG--AEQICVGQNHSDEGA
 HFZ3 YGRVTLPCRRLCQRAYSECSKLMEMFGVPWPEDMECSRFPDCE--EPYPRLVDLNLGAG---
 MFZ3 YGRVTLPCRRLCQRAYSECSKLMEMFGVPWPEDMECSRFPDCE--EPYPRLVDLNLVG---
 HFZ4 INIPIGPCGGMCLSVKRRCEPVLKEFGFAWPESLNCSEKFPQON--DHNHMCMEGPGD----
 MFZ4 INIPIGPCGGMCLSVKRRCEPVLREFGFAWPDTLNCSKFPQON--DHNHMCMEGPGD----
 HFZ5 YHKPLPPCRSVCERAKAGCSPLMRQYGFAPWPERMSCDRLPVLGRDAEVLCDYNRSEATT
 HFZ6 QIHVVPPCRKLCEKVYSDCKKLIDTFGIRWPEELECRLQYCD--ETVPVTFDPHTEF---
 MFZ6 QIHVVLPCKRLCEKIVSDCKKLMDTFGIRWPEELECRLPHCD--DTVPVTFDPHTEF---
 HFZ7 LDQAIPPCRSICERARQGCEALMNKFGFQWPERLRCENFVHG--AGEICVGQNTSDGSG
 MFZ7 LDQAIPPCRSICERARQGCEALMNKFGFQWPERLRCENFVHG--AGEICVGQNTSDGSG
 HFZ8 YKKPLPPCRSVCERAKAGCAPLMRQYGFAPWDRMRCDRLEPQG--NPDTLCMDYNRTDLTT
 MFZ8 YKKPLPPCRSVCERAKAGCAPLMRQYGFAPWDRMRCDRLEPQG--NPDTLCMDYNRTDLTT
 HFZ9 VSTPIACRPMCEQARLRCAPIEQFNFGWPDSDCARLPTRN--DPHALCMEAPENA--TA
 MFZ9 VSTPIACRPMCEQARLRCAPIEQFNFGWPDSDCARLPTRN--DPHALCMEAPENA--TA
 HFZ10 VSTPIACRVMCEQARLKCSPIEQFNFGWPDSDCARLPKN--DPNYLCMEAPNN----
 * : * * : : . . . ** : : * : .

HFZ1 PT---PSLLPEFWTSNPQHGGGGHGRG-----
 MFZ1 PT---PSLLPEFWTSNGQHGGGGYRG-----
 HFZ2 ---PALLTTAPPPGLQPGAGGTPG-----
 HFZ3 ---EPTEGAPV-----A
 MFZ3 ---DPTEGAPV-----A
 HFZ4 ---EE-----V
 MFZ4 ---EE-----V
 HFZ5 APPRPFFAKPTLPG-----PPGA-----PASGG-----
 HFZ6 ---LGPQKKTE-----Q
 MFZ6 ---SGPQKKSD-----Q
 HFZ7 GPGGGPTAYPTAPYLPDLPTALPPG-----
 MFZ7 GAGGSPTAYPTAPYLPDPPTAMSP-----
 HFZ8 AAPSPRRLLPPPPP--GEQPPSGSGHGRPPGARPPHRGGGRGGGGGDAAPARGGGGGGK
 MFZ8 AAPSPRRLLPPPPPPGEQPPSGSGHSRPPGARPPHRGGSSRSGGDAAPPSRGG----K
 HFZ9 GPAEPHKGLGMLPV-----A
 MFZ9 GPTEPHKGLGMLPV-----A
 HFZ10 GSDEPTRGSGLFPP-----L

HFZ1 GFPGGAG----ASERKGFSCPRALKVPSYLYNYHFLGEKDCGAPCEPTKVYGLMYFGPEEL
 MFZ1 GYPGGAG----TVERGKFSCPRALRVPSYLYNYHFLGEKDCGAPCEPTKVYGLMYFGPEEL
 HFZ2 GPGGGGAPPRYATLEHPFHCPVLKVPYSYLYKFLGERDCAAPCEPARPDGSMFFSQEET
 HFZ3 VQRDYG-----FWCPRCLKIDPDLGYSFLHVRDCSPPCP---NMYFR--REEL
 MFZ3 VQRDYG-----FWCPRCLKIDPDLGYSFLHVRDCSPPCP---NMYFR--REEL
 HFZ4 PLPHKTPI-----QPGECHSVGTNSDQYIWKRLNLCVLCGYDAGLY--SRSAK
 MFZ4 PLPHKTPI-----QPGECHSVGSNSDQYIWKRLNLCVLCGYDAGLY--SRSAK
 HFZ5 ECPAGGPFV-----CKCREPFVPIKESHPLYNKVRTGQVPNCAPVCYQPSFSADER
 HFZ6 VQRDIG-----FWCPRHLKTSGGQGYKFLGIDQCAPPCCP---NMYFK--SDEL
 MFZ6 VPRDIG-----FWCPRHLRTSGDQGYRFLGIEQCAPPCCP---NMYFK--SDEL
 HFZ7 ASDGRGRPAF-----PFSCPRQLKVPPYLGYRFLGERDCGAPCEPGRANGLMYFKEEER
 MFZ7 -SDGRGRLSF-----PFSCPRQLKVPPYLGYRFLGERDCGAPCEPGRANGLMYFKEEER
 HFZ8 ARPPGGGAAP---CEPGCQCRAPMVSVSSERHPLYNRVKTGQIANCALPCHNPFFSQDER
 MFZ8 ARPPGGGAAP---CEPGCQCRAPMVSVSSERHPLYNRVKTGQIANCALPCHNPFFSQDER
 HFZ9 PRPARPPG-----DLGPGAGSGTCENPEKFQYVEKSRSCAPRCGPGVEVFWSSRRDK
 MFZ9 PRPARPPG-----DSAPGPGSGGTCNPEKFQYVEKSRSCAPRCGPGVEVFWSSRRDK
 HFZ10 FRPQRPHSAQ---EHPLKDGPGRGCGCDNPGKFHHVEKSASCAPLCTPGVDVYWSREDK

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Figure 8c

HFZ1 RFSRTWIGIWSVLCCASTLFTVLTYLVDMMRRFSYPERPIIFLSGICYTAVAVAYIAGFLLLE
 MFZ1 RFSRTWIGIWSVLCCASTLFTVLTYLVDMPRFSYPERPIISLSGICYTAVAVAYIAGFLLLE
 HFZ2 RFARLWILTWSVLCCASTFFTFTVTLTYLVDMMQRFYPERPIIFLSGICYTMVSVAIYIAGFVLQ
 HFZ3 SFARYFIGLISIIICLSATLFTFLTFLIDVTRFRYPERPIIFYAVCYMMVSLIFFIGFLLLE
 MFZ3 SFARYFIGLISIIICLSATLFTFLTFLIDVTRFRYPERPIIFYAVCYMMVSLIFFIGFLLLE
 HFZ4 EFTDIWMAVWASLCFISTFTVTLTFLIDSSRFSYPERPIIFLSMCYNIYSIAYIVRLTVG
 MFZ4 EFTDIWMAVWASLCFISTFTVTLTFLIDSSRFSYPERPIIFLSMCYNIYSIAYIVRLTVG
 HFZ5 TFATFWIGLWSVLCFISTSTTVATFLIDMDTFRYPERPIIFLSACYLCVSLGFLVRLVVG
 HFZ6 EFAKSFIGHTVSIFCLCATLFTFLTFLIDVRRFRYPERPIIYYSVCYSIVSLMYFIGFLLG
 MFZ6 DFAKSFIGHTVSIFCLCATLFTFLTFLIDVRRFRYPERPIIYYSVCYSIVSLMYFIGFLLG
 HFZ7 RFARLWVGWWSVLCCASTLFTVLTYLVDMMRRFSYPERPIIFLSGICYFMVAVAHVAGFLLLE
 MFZ7 RFARLWVGWWSVLSCASTLFTVLTYLVDMMRRFSYPERPIIFLSGICYFMVAVAHVAGFLLLE
 HFZ8 AFTVFWIGLWSVLCFVSTFATVSTFLIDMERFKYPERPIIFLSACYLFSVVGYLVRVLAG
 MFZ8 AFTVFWIGLWSVLCFVSTFATVSTFLIDMERFKYPERPIIFLSACYLFSVVGYLVRVLAG
 HFZ9 DFALVWMAVWSALCFSTFTVTLTFLLEPHRFQYPERPIIFLSMCYNVYSLAFLIRAVAG
 MFZ9 DFALVWMAVWSALCFSTFTVTLTFLLEPHRFQYPERPIIFLSMCYNVYSLAFLIRAVAG
 HFZ10 RFVAVWLAIWAVLCCFFSFTVTLTFLIDPARFRYPERPIIFLSMCYCVSVGYLIRLRFAG

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|-> extracellular domain loop 1

HFZ1 DRVVCNDK-----FAEDGARTVAQGTKK
 MFZ1 DRVVCNDK-----FAEDGARTVAQGTNK
 HFZ2 ERVVCNER-----FSEDGYRTVVQGTKK
 HFZ3 DRVACNAS-----I---PAQYKASTVTQGSNN
 MFZ3 DRVACNAS-----S---PAQYKASTVTQGSNN
 HFZ4 RERISCDF-----EEAAEPVLIQEGLN
 MFZ4 RERISCDF-----EEAAEPVLIQEGLN
 HFZ5 HASVACS-----RE-----HNHIHYETTGP
 HFZ6 DSTACNKA-----D---EKLELGDTVVLGSQN
 MFZ6 NSTACNKA-----D---EKLELGDTVVLGSNN
 HFZ7 DRAVCVER-----FSDDGRTVAQGTKK
 MFZ7 DRAVCVER-----FSDDGRTVAQGTKK
 HFZ8 HEKVACSGGAPGAGGAGGAGGAAA-GAGAAGAGAGGPGGRGEYEELGAVEQHVRVYETTGP
 MFZ8 HEKVACSGGAPGAGGAGGAGGAAAAGAGAAGRGASSPGARGEYEELGAVEQHVRVYETTGP
 HFZ9 AQSACD-----QEAGALYVIQEGLEN
 MFZ9 AQSACD-----QEAGALYVIQEGLEN
 HFZ10 AESIACD-----RDSGQLYVIQEGLES

←

HFZ1 EGCTILFMMLYFFSMASSIWWVILSLTWFLAAGMKWGHEAIEANSQYFHLAAWAVPAIKT
 MFZ1 EGCTILFMMLYFFSMASSIWWVILSLTWFLAAGMKWGHEAIEANSQYFHLAAWAVPAIKT
 HFZ2 EGCTILFMMLYFFSMASSIWWVILSLTWFLAAGMKWGHEAIEANSQYFHLAAWAVPAVKT
 HFZ3 KACTMLFMVLYFFTMAGSVWVILTITWFLAAVPKWGSEAEIEKKALLFHASAWGIPGTLT
 MFZ3 KACTMLFMVLYFFTMAGSVWVILTITWFLAAVPKWGSEAEIEKKALLFHASAWGIPGTLT
 HFZ4 TGCAIIFLLMYFFGMASSIWWVILTLTWFLAAGLKWGHEAIEMHSSYFHIAAWAIPAVKT
 MFZ4 TGCAIIFLLMYFFGMASSIWWVILTLTWFLAAGLKWGHEAIEMHSSYFHIAAWAIPAVKT
 HFZ5 ALCTIVFLLVYFFGMASSIWWVILSLTWFLAAGMKWGNEAIAAGYQYFHLAAWLIPSVKS
 HFZ6 KACTVLFMLLYFFTMAGTVWVILTITWFLAAGRKWSCEAIEQKAVWFHAWAGTPGFLT
 MFZ6 KACSVVFMVLYFFTMAGTVWVILTITWFLAAGRKWSCEAIEQKAVWFHAWAGTPGFLT
 HFZ7 EGCTILFMVLYFFGMASSIWWVILSLTWFLAAGMKWGHEAIEANSQYFHLAAWAVPAVKT
 MFZ7 EGCTILFMVLYFFGMASSIWWVILSLTWFLAAGMKWGHEAIEANSQYFHLAAWAVPAVKT
 HFZ8 ALCTVVFLLVYFFGMASSIWWVILSLTWFLAAGMKWGNEAIAAGYQYFHLAAWLIPSVKS
 MFZ8 ALCTVVFLLVYFFGMASSIWWVILSLTWFLAAGMKWGNEAIAAGYQYFHLAAWLIPSVKS
 HFZ9 TGCTLVFLLLYFFGMASLLWVVLTLTWFLAAGKKWGHEAIEAHGSYFHMAAWGLPALKT
 MFZ9 TGCTLVFLLLYFFGMASLLWVVLTLTWFLAAGKKWGHEAIEAHGSYFHMAAWGLPALKT
 HFZ10 TGCTLVFLVLYFFGMASLLWVVLTLTWFLAAGKKWGHEAIEANSYFHLAAWAIPAVKT

*: : : : : * * : : : * :

|-> extracellular domain loop 2 ←

HFZ1 ITILALGQVDGDLVSGVCFVLNNVDALRGFVLAPLFVYLFIGTSFLLAGFVSLFRIRTI
 MFZ1 ITILALGQVDGDLVSGVCFVLNNVDALRGFVLAPLFVYLFIGTSFLLAGFVSLFRIRTI
 HFZ2 ITILAMGQIDGDLVSGVCFVLNNVDALRGFVLAPLFVYLFIGTSFLLAGFVSLFRIRTI
 HFZ3 IILLAMNKIEGDNISGVCFVGLYDVALRYFVLAPLCLYVVVGVSLLLAGIISLNRVRIE
 MFZ3 IILLAMNKIEGDNISGVCFVGLYDVALRYFVLAPLCLYVVVGVSLLLAGIISLNRVRIE

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Extracellular domain loop 2 ←

IVILIMRLVDADELDTGLCYVGNQNLDALTGFVAPLFTYLYLIGTLFIAAGLVALFKIRSN
IVILIMRLVDADELDTGLCYVGNQNLDALTGFVAPLFTYLYLIGTLFIAAGLVALFKIRSN
ITALALSSVDGDPVAGICYVGNQNLSLRRFVLGPLVLYLLVGTFLFLLAGFVSLFRIRSV
VMLLAMNKVEGDNISGVCFVGLYDLASRYFVLLPLCLCVFVGLSLLLAGIISLNHVSRQV
VMLLAMNKVEGDNISGVCFVGLYDLASRYFVLLPLCLCVFVGLSLLLAGIISLNHVSRQV
ITILAMQVVDGDLISGVICYVGLSSVDALRGFVLAPLFVYLFIGTSFLLAGFVSLFRIRTI
ITILAMQVVDGDLISGVICYVGLSSVDALRGFVLAPLFVYLFIGTSFLLAGFVSLFRIRTI
IAVLALSSVDGDPVAGICYVGNQSLDNLRGFVLAPLVLYLFIGTMFLLAGFVSLFRIRSV
IAVLALSSVDGDPVAGICYVGNQSLDNLRGFVLAPLVLYLFIGTMFLLAGFVSLFRIRSV
IVILTLRKVAGDELDTGLCYVASTDAAALTGFVLVPLSGYLVLGSSFLLTG FVALFHIRKI
IVVLTLRKVAGDELDTGLCYVASTDPAALTGFVLVPLSCYLVLGTSFLLTG FVALFHIRKI
ILILVMRRVAGDELDTGVICYVGSMDVNALTGFVLIPLACYLVIGTSFILSGFVALFHIRRV
: * : : . * : : * : : . ** : ** : : * : : * : : * : *

→ extracellular domain loop 3

[illegible]

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AIPCPHLQAGGGAPPHPPMSPDFTVFMIKYLMTLIVGITSGFWIWSGKTLNSWRKFYTRL
AIPCPHLQGGGGVPPHPPMSPDFTVFMIKYLMT-----LNSWRKFYTRL
AIPCP-----AHYTPR--MSPDFTVYMIKYLMTLIVGITSGFWIWSGKTLHSWRKFYTRL
HIPCP-----YQVTQMSRPDLILFLMKYLMALIVGIPSVFVWVGSKKTCFEWASFFHGR
HIPCP-----YQVTQMSRPDLILFLMKYLMALIVGIPSIFVWVGSKKTCFEWASFFHGR
-----EMLKIFMSLLVGITSGMWIWSAKTLHTWQ-KCSNR
-----EMLKIFMSLLVGITSGMWIWSAKTLHTWQ-KCSNR
TGQPR----AK-----PEYVWLMLKYFMCLVVGITSGVWIWSGKTVESWRRFTSRC
HIPCP-----YQAKAKARPELALFMIKYLMTLIVGISAVFVWVGSKKTCTEWAGFFKRN
RIPCP-----YQANPKARPELALFMIKYLMTLIVGISAVFVWVGSKKTCTEWAGFFKRN
AVPCP----PGHFPPM---SPDFTVFMIKYLMTMIVGITTGFWIWSGKTLQSWRRFYHRL
AVPCP----PRHFSPM---SPDFTVFMIKYLMTMIVGITTGFWIWSGKTLQSWRRFYHRL
QPDQA----RR-----PDYAVFMLKYFMCLVVGITSGVWVWSGKTLQSWRSLCTR
QPDQA----RR-----PDYAVFMLKYFMCLVVGITSGVWVWSGKTLQSWRSLCTR
AGPGG---RRDCSLPGGSVPTVAVFMLKIFMSLVVGITSGVWVWSKTFQTWQSLCYRK
TVPGG---RRDCSLPGGSVPTVAVFMLKIFMSLVVGITSGVWVWSKTFQTWQSLCYRK
NNQTK---TLDC-LMAASIPAVEIFMVKIFMMLLVVGITSGMWIWTSTLQSWQQVCSRR
      : * : *

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TN--SKQGETTV-----
TN--SKQGETTV-----
TN--SRHGETTV-----
RKKEIVNESRQVLQEP-----DFAQSLLRDPNTPIIRKSRGTSTQGTSTHAS
RKKEIVNESRQVLQEP-----DFAQSLLRDPNTPIIRKSRGTSTQGTSTHAS
LVNSGKVKREKRGNGW-----VKPGKGSE-----
LVNSGKVKREKRGNGW-----VKPGKGNE-----
CC-RPRRGHKSGGA-----MA--AG-D-----
RKRPDISERRVLQESCEFFLKHN SKVKHKKKHYPSSHKLKVISKSMGTSTGATANHGT
RKRPDISERRVLQESCEFFLKHN SKVKHKKKHGAPGPHRLKVISKSMGTSTGATTNHGT

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Figure 8e

HFZ7 SH--SSRGETAV-----
 MFZ7 SH--SSKGETAV-----
 HFZ8 CW-ASKGAAVGGGAGA-----TAAGGGGGPGGGGGGGP
 MFZ8 CW-ASKGAAVGAGAGG-----SGPGGSGP-----GP
 HFZ9 IA--AGRARAKACRAP-----GSYGRGTHC-----
 MFZ9 MA--AGRARAKACRTP-----GGYGRGTHC-----
 HFZ10 LKKKSRRKPASVITSG-----GIYKKAQH-----

HFZ1 -----
 MFZ1 -----
 HFZ2 -----
 HFZ3 STQLAMVDDQRSKAGSIHSKVSSYHGSLHRSRDGRYTPCSYRG--MEERLPHGSMS-RLT
 MFZ3 STQLAMVDDQRSKAGSVHSKVSSYHGSLHRSRDGRYTPCSYRG--MEERLPHGSMS-RLT
 HFZ4 -----TVV-----
 MFZ4 -----TVV-----
 HFZ5 -----YPEASAALTGRTGPPGPAATYHKQVSLSHV-----
 HFZ6 SAVAITSHDYLGQETLTEIQTSPETSMREVKADGASTPRLREQDCGEPASPAASIS-RLS
 MFZ6 SAMAIADHDYLGQETSTEVTSTPEASVKEGRADRANTPSAKDRDCGESAGPSSKLSGNRN
 HFZ7 -----
 MFZ7 -----
 HFZ8 GGGGGPGGGGSLYSDVSTGLTWRSGTAS-SVSYPKQMPLSQV-----
 MFZ8 GGGGGHGGGGSLYSDVSTGLTWRSGTAS-SVSYPKQMPLSQV-----
 HFZ9 -----H---YKAPTIVLHMTKTDPSLENPTHL-----
 MFZ9 -----H---YKAPTIVLHMTKTDPSLENPTHL-----
 HFZ10 -----PQKT-HHGKYEIPAQSPTCV-----

HFZ1 -----
 MFZ1 -----
 HFZ2 -----
 HFZ3 DHSRHSSSHRLNEQSRHSSIRDLSNNPMTHITHGTSMNRVIEEDGTSA-----
 MFZ3 DHSRHSSSHRLNEQSRHSSIRDLSNNPMTHITHGTSMNRVIEEDGTSA-----
 HFZ4 -----
 MFZ4 -----
 HFZ5 -----
 HFZ6 GEQVDGKG--QAGSVSESARSEGRISPKSDITDTGLAQSNLQVPSSSEPSSLKGSTSL
 MFZ6 GRESRAGGLKERSNGSEGAPSEGRVSPKSSVPETGLIDCSTSQAASSPEPTSLKGSTSLP
 HFZ7 -----
 MFZ7 -----
 HFZ8 -----
 MFZ8 -----
 HFZ9 -----
 MFZ9 -----
 HFZ10 -----

HFZ1 -----
 MFZ1 -----
 HFZ2 -----
 HFZ3 -----
 MFZ3 -----
 HFZ4 -----
 MFZ4 -----
 HFZ5 -----
 HFZ6 VHPVSGVRKEQGGGCHSDT
 MFZ6 VHSASRARKEQGAGSHSDA
 HFZ7 -----
 MFZ7 -----
 HFZ8 -----
 MFZ8 -----
 HFZ9 -----

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